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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/603,885	06/26/2000	Stephen William Watson Michnick	Oddy 004	2144

7590 07/22/2003

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EXAMINER
PONNALURI, PADMASHRI

ART UNIT	PAPER NUMBER
1639	

DATE MAILED: 07/22/2003 14

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/603,885	MICHNICK ET AL.	
	Examiner	Art Unit	
	Padmashri Ponnaluri	1639	

-- The MAILING DATE of this communication appears on the cover sh et with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *02 June 2003* .

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1,3-8 and 10-33* is/are pending in the application.

4a) Of the above claim(s) *5-8,10-17 and 20* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1,3,4,18,19 and 21-33* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

11)☐ The proposed drawing correction filed on _____ is: a)☐ approved b)☐ disapproved by the Examiner.

If approved, corrected drawings are required in reply to this Office action.

12)☒ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

13)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____ .

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

14)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).

a) ☐ The translation of the foreign language provisional application has been received.

15)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449) Paper No(s) _____ .
4) ☐ Interview Summary (PTO-413) Paper No(s). _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other:

DETAILED ACTION

1. The amendment B and response filed on 6/2/03 has been fully considered and entered into the application.
2. This application is a continuation-in-part of US Patent application 09/017,412, issued as US Patent 6,70,964 B1; and claims benefit of filing date of provisional application 60/142,210.
3. Claim 9 has been canceled, and claims 1, 3-4 have been amended and new claims 18-33 have been added by the amendment B filed on 6/2/03.
4. Claims 1-8, 10-33 are currently pending in this application.
5. This application contains claims 2, 5-8, 10-17 drawn to an invention nonelected with traverse in Paper No. 11. A complete reply to the final rejection must include cancellation of nonelected claims or other appropriate action (37 CFR 1.144) See MPEP § 821.01.
6. Claim 20 is withdrawn from further consideration pursuant to 37 CFR 1.142(b) as being drawn to a nonelected species (enzyme DHFR is elected as reporter), there being no allowable generic or linking claim. Election was made **without** traverse in Paper No. 11.
7. Claims 1, 3-4, 18-19, 21-33 are currently being examined in this application.
8. The 35 USC 112, second paragraph rejections of record have been withdrawn.
9. The text of those sections of Title 35, U.S. Code not included in this action can be found in a prior Office action.
10. The rejection of claims 1, 3-4 under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for dihydrofolate reductase (DHFR) as reporter

molecule and the use of leucine zipper molecules as panel of molecules in the method of identifying an interacting set of molecules is maintained for the reasons of record.

11. Claims 1, 3-4, 18-19, 21-33 (new claims) are rejected under 35 U.S.C. 102(b) as being anticipated by Pelletier et al (Protein Engineering, 1997, vol. 10, page 89) for the reasons of record.

12. Claims 1, 3-4, 18-19, 21-33 (new claims) are rejected under 35 U.S.C. 102(e) as being anticipated by US Patent 6,270,964 (Michnick et al) for the reasons of record.

13. Claims 1, 3-4, 18-19 and 21-33 (new claims) are rejected under the judicially created doctrine of obviousness-type double patenting over claims 1-41 of U.S. Patent No. 6,270964 for the reasons of record.

Priority

14. Applicants in the response filed on 6/2/03, claim that the instant application is a CIP of 09/017, 412 which is filed on February 1998.

15. Applicant has not complied with one or more conditions for receiving the benefit of an earlier filing date of US patent application for the following reasons:

    a) the later-filed application (US Patent application 09/603,885) is an application filed under 35 U.S.C. 111(a), this reference must also be submitted within the later of four months from the actual filing date of the later-filed application or sixteen months from the filing date of the prior-filed application. These time periods are not extendable. Except as provided in paragraph (a)(3) of this section, the failure to timely submit the reference required by 35 U.S.C. 120 and

paragraph (a)(2)(i) of this section is considered a waiver of any benefit under 35 U.S.C. 120, 121, or 365(c) to such prior-filed application.

b) Claims 1, 3-4, 18-19, 21-33 recite a method for identifying an interacting set of molecules a) by generating first protein fragments and second protein fragments; coupling said protein fragments to a first panel of molecules; coupling the second protein fragments to a second panel of molecules; and mixing the products and identifying the panel members whose interaction resulted in the activity', which were not disclosed in the parent applications, 09/017,412. Applicants refer to US Patent 6,270,964 (US Patent application 09/017,412), Example 7, column 34, lines 12 and further as support for the instant application. However, the section in example 7 refers to a scheme for selection of efficiently heterodimerzing leucine zippers, does not support instantly claimed method for identifying an interacting set of molecules. In a continuation-in-part application, only claims directed solely subject matter adequately disclosed under 35 USC 112, first paragraph in the parent application is entitled to the benefit of the filing date of the parent application. Thus, the instant claims 1, 3-4, 18-33 which recites features not disclosed in the parent applications are entitled only to the filing date of the continuation-in-part application. See MPEP 201.22.

16. The oath or declaration is defective. A new oath or declaration in compliance with 37 CFR 1.67(a) identifying this application by application number and filing date is required. See MPEP §§ 602.01 and 602.02.

The oath or declaration is defective because: If the priority as claimed in the response is granted applicants require new Oath/Declaration identifying the prior documents.

This application presents a claim for subject matter not originally claimed or embraced in the statement of the invention. Applicants with the amendment claim priority to US Patent application. A supplemental oath or declaration is required under 37 CFR 1.67. The new oath or declaration must properly identify the application of which it is to form a part, preferably by application number and filing date in the body of the oath or declaration. See MPEP §§ 602.01 and 602.02.

New Rejections Necessitated by the Amendment

17. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

18. This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

19. Claims 1, 3-4 and 18-19, 21-33 are rejected under 35 U.S.C. 103(a) as being unpatentable over Pelletier et al (Protein Engineering, 1997, 10 (suppl), 89.

Pelletier et al disclose a protein complementation assay for detection of protein-protein interaction in vivo. The reference discloses a protein complementation assay based on reconstitution of DHFR activity. The reference discloses that the direct assay disclosed requires no additional endogenous factors for detecting specific protein-protein interactions. The reference discloses that DHFR is used as reporter enzyme, and GCN4 leucine zippers as model interacting proteins because of their association is well characterized. The reference in

figure 1 discloses that the fragments of reporter molecules interaction with leucine zipper proteins. The reference discloses that the method is useful in identifying protein-protein interactions. The reference specifically teaches that the method is applicable to screening cDNA libraries for the detection of unknown, specific protein-protein interactions.

The reference specifically does not recite library V library screening. However, the reference teaches that GCN4 leucine zippers as model interacting proteins (i.e.,see figures 1-2), and the reference teaches that the in vivo assay could be applied to screening cDNA libraries for the detection of unknown specific protein-protein interactions. Pelletier et al teach panels of mDHFR fragments, see i.e., figure 2, and specifically teach that the disclosed in vivo method could be applied to screening cDNA libraries for the detection of unknown specific protein-protein interactions. Thus it would have been obvious to one skilled in the art at the time the invention was made to use the reference method for in vivo screening of cDNA libraries. A person skilled in the art would have been motivated to use the in vivo method of screening using mDFR taught by Pelletier et al to screen library v library or paenl v panel.

Response to Arguments

20. *The rejection of claims 1, 3-4 and new claims 18-20 under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for dihydrofolate reductase (DHFR) as reporter molecule and the use of leucine zipper molecules as panel of molecules in the method of identifying an interacting set of molecules is maintained for the reasons of record.*

Applicants argue that 'the filing of the above claim amendments that all the rejections and objections under 35 USC. 112, first and second paragraph s have been rendered moot.' Applicants further argue in view that this application now claims CIP status from US serial No. 09/017,412, now US Patent No. 6,270,964, and there is sufficient guidance in the earlier application as to the selection of a reporter molecule as well as sufficient examples of the types of reporters .

Applicants response has been considered but is not persuasive, because of the following reasons: the priority to the US Patent 6,270964 is denied; b) even if the instant application gets the priority of the US patent 6,270,964, which is specifically drawn to the use of DHFR enzyme as a reporter and does not sufficiently teach the use of any other enzyme reporter and leucine zipper as proteins or members of panels.

Applicants arguments regarding CIP status of this application is not persuasive, because the instant application is not filed within the later of four months from the actual filing date of the later-filed application or sixteen months from the filing date of the prior-filed application.

21. Claims 1, 3-4, 18-19, 21-33 are rejected under 35 U.S.C. 102(b) as being anticipated by Pelletier et al (Protein Engineering, 1997, vol. 10, page 89) for the reasons of record.

Pelletier et al disclose a protein complementation assay for detection of protein-protein interaction in vivo. The reference discloses a protein complementation assay based on reconstitution of DHFR activity. The reference discloses that the direct assay disclosed requires no additional endogenous factors for detecting specific protein-protein interactions. The reference discloses that DHFR is used as reporter enzyme, and GCN4 leucine zippers as model interacting proteins because of their association is well characterized. The reference in figure 1 discloses that the fragments of reporter molecules interaction with leucine zipper proteins. The reference discloses that the method is

useful in identifying protein-protein interactions. The reference specifically teaches that the method is applicable to screening cDNA libraries for the detection of unknown, specific protein-protein interactions. The reference clearly anticipates the claimed invention.

Applicants argue that Pelletier et al article describes testing for single protein-protein interactions to determine if the dual fused protein-DHFR fragment would work to reconstitute DHFR and DHFR activity. Applicant's arguments have been considered and are not persuasive because Pelletier et al specifically teach protein complementation assay for detection of protein-protein interactions in vivo. And further reference clearly teaches that the in vivo assay could be applied to screening cDNA libraries for detection of unknown specific protein –protein interactions. Thus, the reference clearly teaches screening libraries. Further applicants arguments 'Pelletier et al article describes testing for single protein-protein interactions to determine if the dual fused protein-DHFR fragment would work to reconstitute DHFR and DHFR activity' are not convincing, because the reference clearly teaches the method steps and the arguments 'testing for single protein-protein interactions' is an intended use. Since the reference has all the claimed method steps the reference clearly anticipates the claimed invention.

22. Claims 1, 3-4 and 18-19, 21-33 (new claims) are rejected under 35 U.S.C. 102(e) as being anticipated by US Patent 6,270,964 (Michnick et al).

Michnick et al disclose protein fragment complementaion assay for the interaction of biological or drug interactions. The reference discloses that the assay can be used to screen cDNA libraries for binding of a target protein with unknown proteins or libraries of small organic molecules for biological activity. Figure 1 in the reference depicts the protein complementation assay. Figure 7 in the reference discloses the method of library versus library screening as the instant claimed method. The reference discloses two semi-random leucine zipper libraries were created and each inserted N-terminal to one of the mDHFR fragments. The reference discloses that the cotrasformation of the resulting zipper-DHFR fragments libraries in E.coli and platting on selective medium allowed for survival of clones harboring successful interacting leucine zippers. Fourteen clones were isolated and the zippers were sequenced to identify the residues at "e" and "g" positions. The "e-g" pairs were categorized as attractive pair and repulsive pair (see column 9, lines 35 to 47). Example 7 of

the reference further discloses the application of the PCA strategy to generate peptides with novel binding properties that may have therapeutic value using two leucine zipper libraries and fragments of mDHFR. Thus the reference clearly anticipates the claimed invention.

Applicant's arguments filed on 6/2/03 have been fully considered but they are not persuasive. Applicants argue that the instant application is a CIP of US Patent 6,270,964 (US patent application 09/017,412) to which priority has not been granted,and the rejections of record have been maintained.

23. Applicant's arguments filed on 6/2/03 regarding the Double patenting rejection have been fully considered but they are not persuasive. Applicants argue that the reference claims do not have method steps directed to the identification of sets of molecules capable of such interations. Applicants arguments are not persuasive, because the reference in claims are drawn to 'a method for detecting biomolecular interactions (refers to protein interactions) with same method steps. Specifically the reference claimed method recites in step c) testing for activity regained by association of the enzyme fragments of the enzyme fragments, wherein said reassociation is mediated by interactions of the second molecules.' And the instant claimed method steps recite 'directly or indirectly testing for association of said activity when said protein fragments are associated and identifying the panel members whose interaction resulted in said activity. Thus, the rejections of record have been maintained for the reasons of record.

24. No claims are allowed.

Conclusion

25. Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

26. A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

27. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Padmashri Ponnaluri whose telephone number is 703-305-3884. The examiner is on Flex schedule and can normally be reached between 7 AM to 3.30 PM on Monday to Friday.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Andrew Wang can be reached on 703-306-3217. The fax phone numbers for the

organization where this application or proceeding is assigned are 703-305-3014 for regular communications and 703-872-9307 for After Final communications.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is 703-308-0916.

Padmashri Ponnaluri
Primary Examiner
Art Unit 1639

July 21, 2003

PADMASHRI PONNALURI
PRIMARY EXAMINER